

1. (Twice Amended) A method of selection and/or identifying one or more protein affinity ligands, wherein the affinity ligands are antibodies, that bind to one or more proteins of interest, comprising the steps of:

(A) obtaining a real or theoretical mass spectrometry based characterization of the one or more proteins by either:

- i. Subjecting the one or more proteins to a mass spectrometry based characterization; or
- ii. Predicting the mass spectrometry based characterization from known data;

(B) utilizing the one or more proteins either individually or as a mixture to:

- i. Generate one or more antibodies thereto by immunization; and/or
- ii. Select, using a single or multiple rounds of binding, one or more antibodies thereto;

(C) screening to one or more antibodies generated in step B(i) and/or multiple antibodies selected by step (B)(ii) by:

- i. adding a mixture of proteins or the one or more proteins individually to the one or more antibodies generated in step (B)(i) or the one or more antibodies selected in step (B)(ii), each antibody being used individually, and
- ii. after removing any proteins which have not bound, eluting the at least one protein has bound;

(D) subjecting the at least one eluted protein to mass spectrometry based characterization; and

Amended

2.
of inter

5
f
7
g
8
t

12. (Once Amended) A method generating monoclonal antibodies to one or more targeted proteins comprising the steps of:

- (a) resolving a complex protein mixture;
- (b) subjecting the resolved protein(s) to peptide mass fingerprinting to obtain a peptide mass profile or obtain a theoretical peptide mass profile;
- (c) utilizing one or more of the resolved proteins to generate one or more monoclonal antibodies thereto;
- (d) adding the or another complex protein mixture to the one or more monoclonal antibodies generated in Step (c), to select those proteins which bind the one or more monoclonal antibodies, and subjecting the selected proteins(s) to peptide mass fingerprinting to obtain a peptide mass profile;
- (e) comparing the peptide mass profiles obtained in steps (b) and (d); and
- (f) selecting one or more monoclonal antibodies of interest.

13. (Once Amended) A method of generating an antibody library comprising the steps of:

- (a) resolving a complex protein mixture and subjecting the resolved protein(s) to peptide mass fingerprinting to obtain a peptide mass profile; or
- (b) obtaining a theoretical peptide mass profile for a protein which is sought;
- (c) utilizing the or the other complex protein mixture to generate one or more monoclonal antibodies thereto;
- (d) adding the one or the other complex protein mixture to the one or more monoclonal antibodies generated in Step (c) to select those proteins which bind

the one or more monoclonal antibodies, and subjecting the selected protein(s) to peptide mass fingerprinting to obtain a peptide mass profile;

- (e) comparing the peptide mass profiles obtained in steps (a or b) and (d); and
- (f) identifying the monoclonal antibodies of interest.

17. (Twice Amended) A method as claimed in claims 1, 2, 7, 8, or 9 wherein the mass spectrometry based characterization is obtained by mass spectrometry.

18. (Twice Amended) A method as claimed in claims 1, 2, 7, 8, or 9 further comprising the use of automated well plate handling technology and automated high-throughput mass spectrometry.

29. (Once Amended) A method as claimed in claim 2 wherein the method is method for selecting and identifying protein affinity ligands to a plurality of proteins.

34. (Once Amended) A method of selecting and/or identifying at least one antibody which binds at least one protein of interest, comprising the steps of:

- (a) obtaining a theoretical mass spectrometry-based characterization of a target protein;
- (b) providing an antibody which selectively binds to said target protein;
- (c) isolating and collecting said target protein through affinity binding with said antibody;

- (d) analyzing said collected target protein for said pre-selected mass spectrometry-based characterization; and
- (e) comparing the mass spectrometry-based characterization obtained in step (d) with the theoretical mass spectrometry-based characterization of step (a).

37. (New) A method as claimed in claim 1 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

38. (New) A method as claimed in claim 37 wherein the eluting agent is formic acid.

39. (New) A method as claimed in claim 8 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

40. (New) A method as claimed in claim 39 wherein the eluting agent is formic acid.

41. (New) A method as claimed in claim 19 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

42. (New) A method as claimed in claim 41 wherein the eluting agent is formic acid.

43. (New) A method as claimed in claim 20 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

44. (New) A method as claimed in claim 43 wherein the eluting agent is formic acid.
45. (New) A method as claimed in claim 21 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.
46. (New) A method as claimed in claim 45 wherein the eluting agent is formic acid.